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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,516	02/10/2000	ERMANNO GHERARDI	1090-26	6832

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[REDACTED] EXAMINER

HAYES, ROBERT CLINTON

[REDACTED] ART UNIT

[REDACTED] PAPER NUMBER

1647

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18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/423,516	Applicant(s) Gherardi et al
Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on Apr 23, 2002.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 31-63 is/are pending in the application.
- 4a) Of the above, claim(s) 42-48 and 55-63 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 31-41 and 49-54 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims 31-63 are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6 & 8 6) Other: _____

Art Unit: 1647

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims 31-41 & 49-54) in Paper No. 17 is acknowledged. The traversal is on the ground(s) that "a search of all the claimed subject matter would not be an undue burden on the Examiner". This is not found persuasive because no special technical feature exists for Group I as defined by PCT Rule 13.2, because it does not define a contribution over the prior art. Note that PCT Rule 13 does not provide for multiple products or methods within a single application. Because the technical feature of Group I is not a special technical feature, and because the technical features of the Group II-IV inventions are not present in the Group I claims, unity of invention is lacking, and therefore, would also be an undue search burden on the Examiner for the art recognized distinct subject matter. The requirement is still deemed proper and is therefore made FINAL.

Claims 42-48 & 55-63 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 17.

This application contains claims 42-48 & 55-63 are drawn to an invention nonelected with traverse in Paper No. 17. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Art Unit: 1647

Sequence Compliance

Note that 37 CFR 1.821 (a)(2)(d) states that each sequence disclosed must appear separately in the “Sequence listing”, and referenced appropriately *in the text of the description* and the claims. See MPEP 2422 & 2431. For example, page 3, line 7, etc. of the specification must be amended to indicate the appropriate SEQ ID NO.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 31-41 & 49-54 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation of "a variant... HGF" encompasses all naturally occurring polypeptides comprising HGF-related proteins; thereby, not involving the hand of man to isolate or purify the polypeptide. It is suggested that amending claims 31, 49 & 54 to "an isolated variant ... HGF polypeptide" should obviate this rejection.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

Art Unit: 1647

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-32 & 49-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the specification describes the human HGF molecule in Figure 7 (i.e., SEQ ID NO:2), no written description of any other HGF sequence is provided in the instant specification. In particular, no polypeptide sequences from other species, allelic variants, splice variants, etc. are adequately described. Therefore, one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of “variant HGF” polypeptides, as encompassed by the claims, because it is unknown and not described what structurally constitutes such generic “variant HGF” polypeptides. Thus, the written description requirements under 35 U.S.C. 112, first paragraph are not met.

Applicant is directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

4. Claims 31-41 & 49-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to HGF variants that are structurally characterized and claimed, does not reasonably provide enablement for any biologically functional equivalent forms of HGF with no recited structural characteristics. The specification

Art Unit: 1647

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The name, HGF variant, does not sufficiently characterize and enable the full scope of the polypeptides encompassed by the current claim language, because the inclusion of any biological functional equivalent protein “which varies in primary amino acid structure from a wildtype form” (pg. 3), etc. within the definition of HGF variant polypeptides sets forth little structural and functional characteristics. Importantly, the specification does not teach which particular amino acids are critical for a generic HGF protein's function; nor how to distinguish HGF variants encompassed by the instant invention from any different HGF-related polypeptides that possesses none of the desired functions of the instant invention. Therefore, any such broadly claimed polypeptides without definable structural characteristics would be expected by the skilled artisan to encode inactive proteins. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for a functional HGF polynucleotide would prevent the skilled artisan from determining whether any random modification or mutation to the single disclosed human HGF

Art Unit: 1647

DNA molecule of SEQ ID NO: 2 could be made which retains the desired function of the instant invention, because any random mutation or modification manifested within a HGF variant protein would be predicted to adversely alter the biologically active 3-dimensional conformation of the HGF protein, without requiring undue experimentation to determine otherwise.

5. Claims 33-41 & 49-54 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is ambiguous what the specific mutations at "amino acid residue R73/ R76/R93E/K78E /K91/K94", etc. entail because no reference sequence is recited in the claims to determine such. For example, different HGF variants and allelic variants from different species do not have the same number of amino acid residues, and variant proteins expressed in eukaryotes usually no longer contain the N-terminal Met residue. It is suggested that amending the claims to reflect specific amino acid positions corresponding to SEQ ID NO. 2 should obviate this particular rejection.

6. Claim 31-41 & 49-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1647

The recitation, “which is *substantially* incapable of binding.... , but which is *capable* of binding...”, is ambiguous because either something binds or it does not bind to a substrate or receptor, respectively. In addition, it is unknown what metes and bounds the relative recitation of “substantially” entails. It is suggested that amending the claims to “which is [substantially] incapable of binding.... , but which is [capable of binding] binds...” would obviate this rejection.

7. Claims 33-35 & 51-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

No proper antecedent basis exists for a “variant *human* ... HGF” in base claims 31 & 49.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31-32 & 34 are rejected under 35 U.S.C. 102(a) as being anticipated by Sakata et al. (IDS Ref. #3).

Art Unit: 1647

Sakata et al. teach a human HGF variant with amino acid substitutions from positively charged amino acid residues at R76 to alanine in a hairpin structure (e.g., pg. 9459; Fig.2), which inherently is “substantially incapable of binding a heparin sulfate proteoglycan” when compared to wildtype HGF or other proteins, yet is “capable of binding to the HGF receptor”; absent evidence to the contrary (i.e., as it relates to claims 31-32 & 34). It is noted that the recitation, “for use in medicine” carrier no patentable weight, and is otherwise redundant.

9. Claims 31-32 & 34 are rejected under 35 U.S.C. 102(a) as being anticipated by Lokker et al. (1994; Suppl. IDS Ref. #37)

Lokker et al. teach a human HGF variant with amino acid substitutions from positively charged amino acid residues at R76, K78, K91, R93 and K94 to alanine in a hairpin structure (e.g., pg.899; Table 1), which inherently is “substantially incapable of binding a heparin sulfate proteoglycan” when compared to wildtype HGF or other proteins, yet is “capable of binding to the HGF receptor”; absent evidence to the contrary (i.e., as it relates to claims 31-32 & 34). It is noted that the recitation, “for use in medicine” carrier no patentable weight, and is otherwise redundant.

Art Unit: 1647

Oath/Declaration

10. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration for Birchmeier. See 37 CFR 1.52(c).

It does not identify the mailing or post office address of each inventor. A mailing or post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing or post office address should include the ZIP Code designation. The mailing or post office address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

(R)✓

Robert C. Hayes, Ph.D.
June 18, 2002

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